

## CLAIMS

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A  
1. A method of determining a biological sample component expression pattern for a biological sample, comprising:

applying a biological sample to an affinity support comprising a ligand coupled to a biological sample-compatible hydrophilic matrix, said ligand comprising a backbone having a plurality of affinity property groups and hydrophilic groups pendent therefrom, and said ligand being configured to at least partially resolve components of a said biological sample;

10 resolving the at least one component of the biological sample to provide thereby an enriched fraction; and

determining a biological sample component expression pattern for the biological sample using the enriched fraction.

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2. The method of claim 1, wherein the biological sample components comprise proteins.

15 3. The method of claim 1, wherein the biological sample components comprise nucleotides.

4. The method of claim 1, wherein said hydrophilic ligand comprises:  
a peptoid backbone; and  
a plurality of affinity property groups and hydrophilic groups being pendent from said peptoid backbone.

20 5. The method of claim 4, wherein said hydrophilic groups are intercalated with said affinity property groups.

6. The method of claim 5, wherein said hydrophilic groups alternate with said affinity property groups along said peptoid backbone.

25 7. The method of claim 6, wherein said affinity property groups are selected from the group consisting of alkyl, (cycloalkyl)alkyl, (cycloheteroalkyl)alkyl, aralkyl, and heteroaralkyl, each substituted optionally from the group consisting of oxo, thia, halo, amino, hydroxy, cyano, nitro, thio, aminocarbonyl, carboxy, and imino.

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8. The method of claim 7, wherein said affinity property groups are selected from the group consisting of methyl, hydroxymethyl, prop-2-yl, 2-methylpropyl, pyrrolidylmethyl, methylthioethyl, 1-hydroxyethyl, thiomethyl, aminocarbonylmethyl, aminocarbonylethyl, carboxymethyl, carboxyethyl, 4-aminobutyl, and 3-guanidinopropyl, guanidinoaryl, hydroxyaryl, amidoalkyl, phosphonyl alkyl, phosphonyl aryl, oligoether, and polyhydroxyalkyl.
9. The method of claim 7, wherein said affinity property groups are selected from the group consisting of optionally substituted aralkyl and heteroaralkyl.
10. The method of claim 9, wherein said affinity property groups are selected from the group consisting of phenylmethyl, hydroxyphenylmethyl, imidazolylmethyl, purinylmethyl, pyrimidinylmethyl, and indolylmethyl.
11. The method of claim 7, wherein said affinity groups are selected from the group consisting of optionally substituted amonioalkyl, trialkylamonioalkyl.
12. The method of claim 7, wherein said affinity property groups are optionally substituted carboxylatoalkyl.
13. The method of claim 4, wherein said hydrophilic groups are selected from the group consisting of alkyloxyalkylenyl, aminoalkyl, alkylaminoalkyl, quaternary ammoniumalkyl, hydroxyalkyl, thioalkyl, alkylthioalkylenyl, carboxyalkyl, alkyloxycarbonylalkyl, and aminocarbonylalkyl.
14. The method of claim 13, wherein said hydrophilic group is alkyloxyalkyl.
15. The method of claim 14, wherein said hydrophilic group is selected from the group consisting of methoxyethyl, hydroxyethyl, 1-hydroxyethyl-2-hydroxyethyl, and 2,3-dihydroxypropyl.
16. The method of claim 4, wherein about 50% of said pendant groups are affinity property groups.
17. The method of claim 16, wherein about 33% of said pendant affinity property groups have a common affinity property.
18. The method of claim 16, wherein about 67% of said pendant affinity property groups have a common affinity property.

19. The method of claim 16, wherein about 100% of said pendant affinity property groups have a common affinity property.

20. The method of claim 4, wherein said affinity property groups and said hydrophilic groups are pendant from nitrogen atoms in the backbone.

5 21. The method of claim 4, wherein said biological sample is derived from a homogeneous source.

22. The method of claim 21, wherein said homogeneous source is a cell line.

23. The method of claim 4, wherein said biological sample is derived from a heterogeneous source.

10 24. The method of claim 23, wherein said heterogeneous source is one or more tissue samples.

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25. ~~The method of claim 23, wherein said heterogeneous source is one or more blood samples.~~

15 26. ~~The method of claim 4, where said hydrophilic peptoid coupled to a hydrophilic biological sample-compatible matrix, is prepared by a procedure comprising:~~

*Doesn't matter? → inorganic synthesis*  
*Doesn't matter limit*  
~~synthesizing a peptoid on a hydrophobic solid phase substrate, said peptoid comprising a peptoid backbone having affinity property and hydrophilic groups pendent therefrom, said peptoid being configured to at least partially resolve biological sample components of a biological sample;  
terminating said peptoid with a chemoselective ligation group;  
cleaving said peptoid from said hydrophobic solid phase substrate; and  
linking said peptoid to a hydrophilic solid phase substrate with the chemoselective ligation group.~~

25 27. ~~The method of claim 4, wherein said hydrophilic peptoid coupled to a hydrophilic biological sample-compatible matrix, is prepared by a procedure comprising:~~

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~~synthesizing a peptoid on a hydrophobic solid phase substrate, said peptoid comprising a peptoid backbone having affinity property and hydrophilic~~

groups pendent therefrom, said peptoid being configured to at least partially resolve biological sample components of a biological sample; and converting said hydrophobic substrate to a hydrophilic substrate.

28. The method of claims 27, wherein said hydrophobic substrate is converted to a hydrophilic substrate by a deprotection reaction removing a hydrophobic protecting group.
29. A method of comparing biological sample phenotypes, comprising:  
determining biological sample component expression patterns for a plurality of biological samples according to the method of claim 1; and  
analyzing differences in biological sample component expression patterns among said biological samples.
30. The method of claim 29, wherein said biological sample components comprise proteins and said analyzing differences comprises determining the presence or absence of one or more of said proteins.
31. The method of claim 30, wherein determining the presence or absence of one or more proteins further comprises determining the abundance of one or more proteins.
32. The method of claim 29, further comprising applying the biological samples to a second peptoid, and analyzing the differences in biological sample component expression patterns determined using each peptoid.
33. The method of claim 29, wherein one of said biological samples is derived from a healthy tissue sample and another of said biological samples is derived from a diseased tissue sample.
34. The method of claim 29, wherein one of said biological samples is derived from a healthy tissue sample of a first type and another of said biological samples is derived from a diseased tissue sample of the same cell type.
35. The method of claim 29, wherein one of said biological samples is derived from a diseased tissue sample of a first type and another of said biological samples is derived from a diseased tissue sample of a second type.

36. A method of reducing the complexity of a biological sample, comprising:  
applying the biological sample to a hydrophilic affinity support as described in  
claim 1; and

fractionating biological sample components of the biological sample using the  
hydrophilic support.

37. The method of claim 36, further comprising selecting an affinity support for  
reducing the complexity of the biological sample, comprising:

applying a portion of the biological sample to each of a plurality of affinity  
supports, said plurality of affinity supports comprising an array of peptoids  
configured to at least partially resolve biological sample components, which  
peptoids are coupled to biological sample-compatible matrixes;

identifying differences in complexity reduction achieved by different the  
supports; and

selecting a support using said differences.

38. The method of claim 37, wherein said plurality of affinity supports is provided  
in one or more multi-compartment containment structures.

39. The method of claim 38, wherein said plurality of affinity supports is  
provided in a plurality of multi-compartment containment structures.

40. The method of claim 36, further comprising at least one of identification and  
quantitation of the components of the biological sample.

41. The method of claim 40, wherein said identification and/or quantitation  
includes mass spectral analysis.

42. The method of claim 39, comprising:

applying said biological sample to a first multi-compartment containment  
structure wherein one or more compartments contains a plurality of affinity  
supports;

identifying differences in complexity reduction achieved by supports in  
different compartments of the first multi-compartment containment structure;

selecting a support-containing compartment from the first multi-compartment containment structure using said differences;

applying said biological sample component mixture sample to a second multi-compartment containment structure wherein separate compartments contain the one or more supports from said selected support-containing compartment from the first multi-compartment containment structure;

identifying differences in complexity reduction achieved by different supports of the selected support-containing compartment from the first multi-compartment containment structure; and

selecting a support from the array and represented in said second multi-compartment containment structure using said differences.

43. A kit for reducing the complexity of a biological sample, comprising:  
a plurality of affinity supports, said plurality of affinity supports comprising an array of hydrophilic ligands coupled to biological sample-compatible matrixes as described in claim 1, said hydrophilic ligands coupled to biological sample-compatible matrixes being provided in separate compartments of a multi-compartment containment structure.

44. The kit of claim 43, wherein each of said hydrophilic ligands comprises:  
a peptoid backbone; and  
a plurality of affinity property groups and hydrophilic groups being pendent from said peptoid backbone.

45. The kit of claim 44, wherein said multi-compartment containment structure comprises a well plate.

46. The kit of claim 45, wherein said well plate is a fritted well plate.

47. The kit of claim 44, wherein said multi-compartment containment structure comprises a patterned chip.

48. The kit of claim 47, wherein said chip comprises a substrate of a material selected from Si, Au, Al and glass.

49. A hydrophilic peptoid, comprising:

a peptoid backbone; and

a plurality of affinity property groups and hydrophilic groups being pendent from said peptoid backbone;

wherein about 50% of said pendant groups are affinity property groups.

5 50. The peptoid of claim 49, wherein about 33% of said pendant affinity property groups have a common affinity property.

51. The peptoid of claim 49, wherein about 67% of said pendant affinity property groups have a common affinity property.

10 52. The peptoid of claim 49, wherein about 100% of said pendant affinity property groups have a common affinity property.

53. The peptoid of claim 49, wherein said hydrophilic groups are intercalated with said affinity property groups.

54. The peptoid of claim 53, wherein said hydrophilic groups alternate with said affinity property groups along said peptide backbone.

15 55. The peptoid of claim 49, wherein said peptoid is coupled to a biological sample-compatible matrix using a chemoselective ligation group.

56. The method of claim 4, where said hydrophilic peptoid coupled to a hydrophilic biological sample-compatible matrix, is prepared by a procedure comprising:

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20 synthesizing a peptoid on a hydrophobic solid phase substrate, said peptoid comprising a peptoid backbone having affinity property and hydrophilic groups pendent therefrom wherein about 50% of said pendant groups are affinity property groups, said peptoid being configured to at least partially resolve biological sample components of a biological sample;

25 terminating said peptoid with a chemoselective ligation group;

cleaving said peptoid from said hydrophobic solid phase substrate; and

linking said peptoid to a hydrophilic solid phase substrate with the chemoselective ligation group.

57. The method of claim 56, wherein about 33% of said pendant affinity property groups have a common affinity property.

58. The method of claim 56, wherein about 67% of said pendant affinity property groups have a common affinity property.

5 59. The method of claim 56, wherein about 100% of said pendant affinity property groups have a common affinity property.

60. The method of claim 4, wherein said hydrophilic peptoid coupled to a hydrophilic biological sample-compatible matrix, is prepared by a procedure comprising:

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10 synthesizing a peptoid on a hydrophobic solid phase substrate, said peptoid comprising a peptoid backbone having affinity property and hydrophilic groups pendent therefrom wherein about 50% of said pendant groups are affinity property groups, said peptoid being configured to at least partially resolve biological sample components of a biological sample; and

15 converting said hydrophobic substrate to a hydrophilic substrate.

61. The method of claim 60, wherein about 33% of said pendant affinity property groups have a common affinity property.

62. The method of claim 60, wherein about 67% of said pendant affinity property groups have a common affinity property.

20 63. The method of claim 60, wherein about 100% of said pendant affinity property groups have a common affinity property.

64. The method of claims 60, wherein said hydrophobic substrate is converted to a hydrophilic substrate by a deprotection reaction removing a hydrophobic protecting group.

25 65. A method of processing a biological sample, comprising:  
applying a biological sample to a plurality of affinity supports, each of said supports comprising a hydrophilic ligand, said ligand coupled to a biological sample-compatible hydrophilic matrix, said ligand comprising a plurality of affinity property groups and hydrophilic groups being pendent from a



backbone, and being configured to at least partially resolve biological sample components of a biological sample; and

in parallel, fractionating components of the sample using the affinity supports to generate enriched fractions.

5 66. The method of claim 65, wherein said enriched fractions comprise portions of the biological sample that does not bind to the affinity supports.

67. The method of claim 65, wherein said enriched fractions comprise portions of the biological sample that initially bind to the affinity supports.

10 68. The method of claim 67, wherein said enriched fractions comprise portions of the biological sample that are eluted from the affinity supports as a single elution fraction.

69. The method of claim 67, wherein said enriched fractions comprise portions of the biological sample that are eluted from the affinity supports as a plurality of elution fractions.

15 70. The method of claim 65, wherein each of said hydrophilic ligands comprises:  
a peptoid backbone; and  
a plurality of affinity property groups and hydrophilic groups being pendent from said peptoid backbone.

20 71. A method of processing a biological sample, comprising:  
applying the biological sample to a first affinity support comprising a hydrophilic ligand, said ligand coupled to a biological sample-compatible hydrophilic matrix, said ligand comprising a plurality of affinity property groups and hydrophilic groups being pendent from a backbone, and being configured to at least partially resolve components of a biological sample  
25 according to a first affinity interaction with said biological sample;  
fractionating components of the biological sample using the first affinity support to provide an enriched fraction;  
applying the enriched fraction to a second affinity support comprising a hydrophilic ligand, said second ligand coupled to a biological sample-

compatible hydrophilic matrix, said ligand comprising a plurality of affinity property groups and hydrophilic groups being pendent from a backbone, and being configured to at least partially resolve components of a biological sample according to a second affinity interaction with said biological sample; and

fractionating biological sample components of the enriched sample fraction using the second affinity support to provide a twice enriched fraction.

72. The method of claim 71, wherein each of said hydrophilic ligands comprises:  
a peptoid backbone; and  
a plurality of affinity property groups and hydrophilic groups being pendent from said peptoid backbone.

73. The method of claim 71, further comprising one or more additional applications and fractionations of a previously enriched fraction using one or more additional affinity supports, each of said one or more additional supports comprising a hydrophilic ligand said one or more additional ligands coupled to a biological sample-compatible hydrophilic matrix, said one or more additional ligands comprising a plurality of affinity property groups and hydrophilic groups being pendent from a backbone, and being configured to at least partially resolve components of a biological sample according to an additional affinity interaction with said previously enriched fraction.

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